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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte CHERYL D. BLUME and ANTHONY R. DISANTO

Appeal 2007-001080
Application 10/790,658
Technology Center 1600

Decided: May 25, 2010

Before JAMES T. MOORE, *Vice Chief Administrative Patent Judge*, and LORA M. GREEN, and RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON REHEARING

Appellants request a rehearing under 37 C.F.R. § 41.52 of the "Vacatur and Remand" entered March 26, 2007 (hereinafter, "Remand").

Statement of the Case

Pending claims 26 and 34-62 involve the treatment of immune dysfunction associated with reduced levels of γ-interferon comprising administering the (R)(-) enantiomer of desmethylselegeline.

Claim 26 reads as follows:

26. A method of treating a condition in a mammal produced by immune system dysfunction that is associated with reduced levels of γ-interferon production, which comprises administering to the mammal the R(-) enantiomer of desmethylselegiline, or a pharmaceutically acceptable acid addition salt thereof, at a daily dose, administered in a single or multiple dosage regimen, of at least about 0.015 mg, calculated on the basis of the free secondary amine, per kg of the mammal's body weight, wherein the administration of the R(-) enantiomer of desmethylselegiline or a pharmaceutically acceptable acid addition salt thereof leads to an increase in γ-interferon production in the mammal.

The claims were rejected by the Examiner under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement, and under 35 U.S.C. § 103(a) as obvious in view of Borbe,[1] Barton, [2] and Balsa[3] (Ans. 3 & 7). Appellants appealed the Examiner's decision (App. Br. 8).

After considering the basis of the rejections as set forth in the Answer, we vacated and remanded the Appeal back to the Examiner because certain issues had not been addressed. Appellants have responded to our action by

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[1] H.O. Borbe et al., *Kinetic evaluation of MAO-B-activity following oral administration of selegiline and desmethyl-selegiline in the rat*, Journal of Neural Transmission, 32:131-137 (1990).
[2] Norman W. Barton et al., *Neurological complications of Kaposi's sarcomat*, Journal of Neuro-Oncology, 1: 333-346 (1983).
[3] D. Balsa et al., *Monoamine Oxidase Activities in Lymphocytes and Granulocytes taken from pig blood*, Biochemical Pharmacology, 36:2273-2728 (1987).

filing a Request for Rehearing ("Request") which provided arguments as to why these issues do not raise patentability concerns.

Upon reconsideration, we modify the "Vacatur and Remand" as follows:

1. The rejection of claims 26 and 34-62 under § 112 is reversed.

2. The rejection of claims 26 and 34-62 under § 103 as obvious in view of Borbe, Barton, and Balsa is reversed.

3. A new ground of rejection under § 103(a) is made in view of Milgram (U.S. Pat. 5,387,615, issued Feb. 7, 1995) and Borbe.

REJECTION UNDER § 112, FIRST PARAGRAPH

Claims 26 and 34-62 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

Statement of the issue

The issue in this rejection is whether the Examiner provided sufficient reasons to doubt the scope of enablement for the claimed subject matter.

Principles of Law

"'[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech, Inc. v. Novo Nordisk*, A/S, 108 F.3d 1361, 1365, (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993)).

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the

specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement . . . *Marzocchi*, 439 F.2d at 223-24." *In re Wright*, 999 F.2d at 1561-62.

Facts ("F")

1. Example 11 in the Specification "shows that there is a sharp decline in cellular [γ-]interferon production that occurs with age." (Spec. 39:9-20.)

2. Example 11 demonstrated that administration of R(-)-desmethylselegiline "led to a restoration" of γ-interferon levels associated with age (*id.* at 39-40).

3. As "IFN-γ production is associated with the ability to successfully recover from infection with viruses and other pathogens," the Specification asserted that R(-)-desmethylselegiline would have "a therapeutically beneficial effect for diseases and conditions mediated by weakened host immunity," including "AIDS, response to vaccines, infectious diseases and adverse immunological effects caused by cancer chemotherapy." (*Id.* at 41:1-6).

Analysis

Claim 26 is drawn to a "method of treating a condition in a mammal produced by immune system dysfunction that is associated with reduced levels of γ-interferon production" comprising administering R(-)-desmethylselegiline, or a pharmaceutically acceptable addition salt of it. (Claim 26.) The administered R(-)-desmethylselegiline "leads to an increase in γ-interferon production in the mammal." (*Id.*)

The Examiner found that the claims broadly covered immune system dysfunction without restriction to a particular condition or disease (Ans. 4.) The Examiner contends that immune system function is "complex" and that

a reduction in γ-interferon does not necessary lead to immune system dysfunction in all cases (*id.*) The Examiner further contends that the Specification did not provide evidence that the R(-)-desmethylselegiline was useful for "treating any or all disorders produced by immune dysfunction," and therefore is not enabled for the full scope of the claims (*id.* at 6).

The Examiner did not provide sufficient reasons for doubting the assertions in the Specification as to the scope of enablement. The claims do not cover "any or all disorders produced by immune dysfunction" as found by the Examiner, but rather are directed to those conditions "associated with reduced levels of γ-interferon production." (Claim 26.) The Specification performed experiments in which aging, a condition associated with reduced γ-interferon, was treated with R(-)-desmethylselegiline. The treatment restored the interferon levels (F1 & F2).

In view of the ability of R(-)-desmethylselegiline to restore γ-interferon levels, the Specification asserted that the compound would be beneficial for other diseases associated with reduced γ -interferon (F3). This assertion was fact-based and scientific. In their Appeal Brief, Appellants cited additional evidence from the published literature that γ-interferon deficiency had been recognized in immune and autoimmune diseases, providing further evidence of the credibility of their assertions (App. Br. 11). The Examiner did not identify a defect in the reasoning set forth in the Specification nor provide a scientific basis on which to doubt it.

In our Remand, we acknowledged that the prior art, as established by Billiau,[4] taught that γ-interferon was known to play an important regulatory role in the immune response (Remand 3). However, we found:

> Billiau reports that gamma-interferon stimulated rather than inhibited HIV viral replication (Billiau at 96). This seems to suggest that increasing gamma-interferon levels to treat AIDS as recited in claims in claims [sic] 37 and 60 would enhance the disease, rather than ameliorate it.

(*Id.*)

Appellants responded to this concern in their Request. They cited scientific publications which indicated that γ-interferon played different roles in the regulation of HIV depending on the infected cell type (*id.* at 5). Furthermore, evidence was provided that γ-interferon had been used to treat HIV infection (*id.* at 4-5), further supporting the credibility of their assertions.

We conclude that Appellants provided adequate evidence to establish that persons of ordinary skill in the art would have reasonably believed that R(-)-desmethylselegiline would raise γ-interferon levels, ameliorating AIDS in at least some HIV-infected patients.

The Remand also raised concerns about cancer treatment in claims 38 and 61 in view of Billiau's report of studies in which gamma-interferon enhanced tumor growth (Remand 3).

In the Request, Appellants provided evidence from 13 publications that "cancer patients in a number of different clinical trials have responded positively to interferon-γ treatment." (Request 5.)

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[4] Alfons Billiau, *Interferon-γ: Biology and Role in Pathogenesis, Advances in Immunology*, Vol. 62, 61-130 (1995).

This evidence established that persons of ordinary skill in the art would have reasonably believed that raising γ-interferon levels as claimed would be successful in treating cancer. While all types of cancer might not respond, the evidence of record establishes that persons of ordinary skill in the art were familiar with testing for the efficacy of γ-interferon in cancer treatment and would have routinely determined those patients who responded to treatment from those did not.

For the reasons set forth above, we conclude that there was insufficient reason to doubt the scope of enablement for the claimed treatment methods. The rejection under § 112, first paragraph is reversed.

OBVIOUSNESS REJECTION

Claims 26 and 34-62 stand rejected under 35 U.S.C. § 103(a) as obvious in view of Borbe, Barton, and Balsa.

Statement of the issue

The issue in this rejection is whether the Examiner provided adequate reasoning to establish that persons of ordinary skill in the art would have combined the disclosures of Borbe, Barton, and Balsa to have made the claim method of treating immune system dysfunction with R(-) desmethylselegiline.

Principles of Law

"During [patent] examination, the examiner bears the initial burden of establishing a *prima facie* case of obviousness." *In re Kumar*, 418 F.3d 1361, 1366 (Fed. Cir. 2005).

In making an obviousness determination, "there must be some articulated reasoning with some rational underpinning to support the legal

conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006); (*see also KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (It "can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.")).

Analysis

The Examiner has the burden of establishing a prima facie case of obviousness. To meet that burden, a reason must be provided, with "some rational underpinnings," that would have prompted persons of ordinary skill in the art to have modified the prior art to have made the claimed invention. *In re Kahn*, 441 F.3d at 988; *KSR*, 550 U.S. at 418.

The Examiner found that Borbe taught that desmethylselegiline ("DMS") blocked MAO-B, but acknowledged that it had not been used to treat immune system dysfunction as required by all the claims (Ans. 7). However, the Examiner found that Balsa reported that MAO-B was expressed in lymphocytes and granulocytes (*id.*). The Examiner concluded:

> it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use DMS of Borbe for reducing the MAO-B activity in lymphocytes and granulocytes, . . . because Barton associates immune dysfunction with conditions such as AIDS, Kaposi's' [sic] sarcoma etc., and Balsa teaches that activity of MAO-B is predominant in G and L cells.

(Ans. 8).

The Examiner did not provide a sufficient reason as to why persons of ordinary skill in the art would have treated the immune disorders described in Barton with the R(-) desmethylselegiline. Specifically, there was no evidence cited in the Answer that one of ordinary skill in the art would have

recognized or expected that inhibiting MAO-B activity in lymphocytes and granulocytes with R(-) desmethylselegiline would have treated immune dysfunction associated with the reduced levels of γ-interferon. The mere presence of the MAO-B enzyme in lymphocytes and granulocytes is insufficient to establish that the enzyme has a role in immune disorders. Absent such evidence, we agree with Appellants that the rejection should be reversed.

NEW GROUND OF REJECTION

Claim 26 is rejected under 35 U.S.C. § 103(a) as obvious in view of Milgram and Borbe. This a new ground of rejection under 37 C.F.R. § 41.50(b).

Facts

4. Milgram describes treating immune dysfunction in mammals with L-deprenyl, an MAO-B inhibitor, at a dosage of 0.1 mg/kg to 5.0 mg/kg (Milgram, col. 1, ll. 15-16; col. 2, ll. 60-65; col. 4, ll. 1-5; & col. 6, ll. 36-39). L-deprenyl is also known as selegiline.

5. Borbe teaches that selegiline and R(-)-desmethylselegiline inhibit MAO-B activity (Borbe, Abstract; pp. 135-36).

Analysis

In the Remand, we noted that the instant Specification disclosed the Milgram patent which described the use of selegiline, an inhibitor of MAO-B, for treating immune system dysfunction (F4). In view of Milgram's teaching that selegiline is useful to treat immune dysfunction and Borbe's teaching that both selegiline and R(-)-desmethylselegiline are MAO-B inhibitors (F5), persons of ordinary skill in the art would have reasonably expected that the R(-)-desmethylselegiline would also be effective in treating

immune dysfunction. As both compounds had been investigated by Borbe for their pharmacological activity, persons of ordinary in the art would have had reason to have substituted R(-)-desmethylselegiline for selegiline as a pharmacological agent in Milgram's method.

Appellants argued that Milgram taught dosages of between 0.1 mg/kg and 5.0 mg/kg of body weight of selegiline, but claim 26 (and dependent claims 34-39 and 42), claim 43 (and dependent claims 44 and 45), and claim 57 recite a dosage of at least 0.015 mg/kg of the R(-)-desmethylselegiline, which is between 6 and 7-fold lower than the dosage taught by Milgram (Request 4; F4). Based on Borbe's teachings, Appellants argued that R(-)-desmethylselegiline would have been expected to be less therapeutically effective as selegiline, "thus limiting or eliminating the potential usefulness of R(-)-desmethylselegiline as a pharmaceutical compound." (*Id.* at 14.)

We agree with Appellants that there is no teaching in Milgram or Borbe which would have led persons of ordinary skill in the art to administer dosages of 0.015 mg/kg of (R)(-)-desmethylselegiline to treat immune dysfunction. However, claim 26 has no upper dosage limit and therefore encompasses much higher dosages than 0.015 mg/kg, including the amounts disclosed in Milgram. Therefore, even were (R)(-)-desmethylselegiline expected to have less activity than selegiline, and thus to require higher dosages to achieve a therapeutic effect, such dosages would still fall within the scope of claim 26 which recites no upper limit. A method claim is unpatentable under § 103 if any scope of it would have been obvious to a person of ordinary skill in the art at the time the invention was made.

Appellants' contention that reduced activity of (R)(-)-desmethylselegiline would have eliminated its use as a pharmaceutical

compound is not supported by the evidence. Borbe expressly teaches that (R)(-)-desmethylselegiline possesses a pharmacological activity, albeit equipotent or less than selegiline.

Finally, Appellants argue that unexpected results were obtained with (R)(-)-desmethylselegiline, but did not provide supporting evidence commensurate with the scope of the claim. "An applicant cannot prove unexpected results with attorney argument and bare statements without objective evidentiary support." *CFMT Inc. v. Yieldup Inter'l41.50 Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003).

We have not reviewed any of the remaining pending claims to the extent necessary to determine whether these claims are unpatentable over the applied prior art references and other reference cited in the record.

TIME PERIOD FOR RESPONSE

This decision contains a new ground of rejection pursuant to 37 C.F.R. § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 C.F.R. § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 C.F.R. § 41.50(b) also provides that the Appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) Reopen prosecution. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the

> Examiner, in which event the proceeding will be remanded to the Examiner. . .
> (2) Request rehearing. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

GRANTED; REVERSED; 37 C.F.R. § 41.50(b)

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